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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LIU, SAMUEL W	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 10/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/684,215	SKEIKY ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,11,13-16,27,28 and 31-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 10-11, 13-16, 27-28 and 31-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1-6, 10-11, 13-16, 27-28 and 31-40 are pending.

It is of note that claims 7-9, 12, 17-26 and 29-30 have been canceled by applicants' amendment filed 8 August 2003. Claims 1-6, 10-11, 13-16, 27-28, 31-40 are thus examined in this Office action.

Note that grounds of objection and/or rejection not explicitly restated and/or set forth below are withdrawn, and that the text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

This application claims priority to provisional application No. 60/158585 filed 7 October 1. The priority application does not disclose the instant SEQ ID NO:18 which the instant SEQ ID NOs:4 and 23 does not comprise and from which the instant SEQ ID NOs:4 and 23 differ. As such, the claims with respect to SEQ ID NO:18 of the instant application are not entitled to the benefit of the tiling date of 06/158585.

Claim Rejections - 35 USC §102

The rejection is restated as follows.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C.

122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The claims 1-5, 10-11, 14-16, 27-28, 31 and 33, 35 and 37-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Wang et al. (US Pat. No. 6509448).

In Example 10, Wang et al. teach a cDNA (SEQ ID NO:1861) encoding a bi-fusion protein comprises a full-length Ra12 polypeptide and a non-*M. tuberculosis* polypeptide which is tumor antigens L801P ORF4 or L801P ORF5.

Wang's SEQ ID NO:1861 depicts the nucleic acid sequence (Ra12:ORF5) encoding bi-fusion protein of amino acid sequence of SEQ ID NO:1863, which shows that Ra12 extends from residue 8 (Thr) to residue 135 (Ala) and a non- *M. tuberculosis* polypeptide from residue 206 (Met) to residue 314 (Arg) encoded by L801P ORF5, wherein the Ra12 nucleotide sequence is 5' to ORF5.

Wang's SEQ ID NO: 1862 depicts the nucleic acid sequence (Ra12:ORF4) encoding bi-fusion protein of amino acid sequence of SEQ ID NO:1864; SEQ ID NO: 1863 which shows that Ra12 extends from residue 8 (Thr) to residue 135 (Ala) and a non- *M. tuberculosis* polypeptide from residue 137 (Gly) to residue 273 (Gln) encoded by L801P ORF4, wherein the Ra12 nucleotide sequence is 5' to ORF4.

Upon perusal of SEQ ID NO: 1861 and 1862, it is noted that Example 10 reverses these sequences.

The full-length Ra12 (encoded by SEQ ID NO:1861 or SEQ ID NO:1862) is identical to the instant SEQ ID NO:18; and instant SEQ ID NO: 17 is a subsequence of SEQ ID NO:18 from amino acid residues 1 to 30 of SEQ ID NO:18. Wang et al. teaches that Ra12 enhances the

expression and/or immunogenicity of heterologous polynucleotide/polypeptide sequences (see column 53, lines 17-58). Thus, the above Wang et al. teaching anticipates the claims 1-2, 10-11 and 37-38 of the current application.

Wang et al. teach that the Ra12 polynucleotide sequence is located 5' to the non-*M. tuberculosis* polynucleotide sequence, as applied to the instant claim 2; wherein the non-*M. tuberculosis* polynucleotide sequence is an eukaryotic polypeptide, as applied to the instant claims 33 and 35.

Wang et al. teach the linker sequence is "Glu-Phe" in the Ra12:ORF4 sequence (SEQ ID NO: 1864), and a linker sequence from residue 136 (Glu) to residue 205 (Gly) in the Ra12:ORF5 sequence (SEQ ID NO: 1863). Thus, SEQ ID NOs: 1862 and 1861 have coding sequence for the linker peptides between Ra12 and ORF4 or ORF5, as applied to the instant claim 3.

Wang et al. teach at least one trypsin cleavage site (e.g., Ala-Arg-Asn) existing in the linker sequence encoded by Ra12:ORF5, and thus the linker peptide comprises a cleavage site, as applied to the instant claim 4.

Since each fusion protein comprises a poly-His sequence at its N-terminus (see SEQ ID NO:1863); thus, the nucleic acid encodes a fusion protein comprising an affinity tag, as applied to the instant claim 5.

At Example 10, Wang et al. further teach nucleic acid sequences of SEQ ID NO:1861 were cloned in expression vector pCRX1 (Claim 14), and expressed from *E. coli* host cell (HMS174(DE3)pLysS strain), as applied to the instant claims 15-16, 27-28 and 31.

Claim Rejections - 35 USC §103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 13, 27, 32, 34, 36 and 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang T. et al. (US Pat. No. 6509448) taken with Reed, S. G. et al. (US Pat. No. 6627198).

In Example 10, Wang et al. teach a cDNA (SEQ ID NO:1861) encoding a bi-fusion protein comprises a full-length Ra12 polypeptide and a non-*M. tuberculosis* polypeptide which is tumor antigens L801P ORF4 or L801P ORF5.

Wang's SEQ ID NO:1861 depicts the nucleic acid sequence (Ra12:ORF5) encoding bi-fusion protein of amino acid sequence of SEQ ID NO:1863, which shows that Ra12 extends from residue 8 (Thr) to residue 135 (Ala) and a non- *M. tuberculosis* polypeptide from residue 206 (Met) to residue 314 (Arg) encoded by L801P ORF5, wherein the Ra12 nucleotide sequence is 5' to ORF5.

Wang's SEQ ID NO: 1862 depicts the nucleic acid sequence (Ra12:ORF4) encoding bi-fusion protein of amino acid sequence of SEQ ID NO:1864; SEQ ID NO: 1863 which shows that Ra12 extends from residue 8 (Thr) to residue 135 (Ala) and a non- *M. tuberculosis* polypeptide

from residue 137 (Gly) to residue 273 (Gln) encoded by L801P ORF4, wherein the Ra12 nucleotide sequence is 5' to ORF4.

Upon perusal of SEQ ID NO: 1861 and 1862, it is noted that Example 10 reverses these sequences.

Thus, Wang et al. teaches nucleic acid encoding a fusion protein comprising Ra12 and a non-*M. tuberculosis* polynucleotide, wherein the Ra12 polypeptide consists of SEQ ID NO: 17 or NO: 18. In Example 10, Wang tel. Further teach that nucleic acid sequences SEQ ID NO:1861 and SEQ ID NO: 1862 were placed in expression vector pCRX1 and expressed from a *E. coli* host cell (HMS174(DE3)pLysS).

Wang et al. do not teach that Ra12 consists of SEQ ID NO: 4 or its subsequence SEQ ID NO: 23.

In the Example at column 20, Reed et al. teach Ra12 having instant SEQ ID NO: 4 and NO: 23 in a bi-fusion polypeptide comprising two *M. tuberculosis* antigens (see Reed SEQ ID NO: 27 and SEQ ID NO: 28). These bi-fusion polypeptides were able to induce T-cell proliferation in peripheral blood mononuclear cells preparations (see column 21, lines 45-63).

It would have been obvious to a person having ordinary skill in the art to substitute the Ra12 of Reed from the Ra12 of Wang because Wang et al. teach that Ra12 enhances the immunogenicity of heterologous polynucleotide/polypeptide sequences (note that ORF4 and ORF5 are lung tumor antigens), and Reed et al. demonstrated that the Ra12 having SEQ ID NO: 4 or NO: 23 is useful for inducing T-cell proliferation, and thus enhances immunogenicity. Thus, the above Wang's teaching are applied to the instant claims 1, 13, 32 and 39.

It would have been obvious to a person having ordinary skill in the art to recombinantly produce a fusion protein comprising the Ra12 of Reed and the non- *M. tuberculosis* antigen encoded by Wang's L801P ORF4 or L801P ORF5 because Wang et al. teach the Ra12 fusion has advantage of enhancing the expression and immunogenicity of heterologous polynucleotide /polypeptide sequences (see column 53, lines 17-22). Thus, the above Wang et al. teachings are applied to the instant claims 27, 34, 36 and 40. Note that characterization of the expression includes step of isolation or purification of the fusion protein.

Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang T. et al. (US Pat. No. 6509448) as applied to claim 1 above, and further in view of Watson, M. A. et al. (US Pat. No. 6566072).

In Example 10, Wang et al. teach fusion proteins comprising full-length Ra12 and lung tumor antigens L801P ORF4 or L801P ORF5. The full-length Ra12 is in the instant SEQ ID NO:18, and instant SEQ ID NO: 17 is a subsequence of SEQ ID NO: 18 from amino acid residue 1 to 30 if SEQ ID NO: 18. Wang et al. teach that the Ra12 enhances the expression and/or immunogenicity of heterologous polynucleotide/polypeptide sequences (see column 53, lines 17-58).

Wang's SEQ ID NO: 1861 depicts the nucleic acid sequence encoding Ra12:ORF5; SEQ ID NO: 1864 shows that Ra12 extends from 8Thr to Ala135 and L801P ORF4 from Gly137 to Gln273.

Wang's SEQ ID NO: 1862 depicts the nucleic acid sequence (Ra12:ORF4) encoding bi-fusion protein of amino acid sequence of SEQ ID NO:1864; SEQ ID NO: 1863 which shows that

Ra12 extends from residue 8 (Thr) to residue 135 (Ala) and a non- *M. tuberculosis* polypeptide from residue 137 (Gly) to residue 273 (Gln) encoded by L801P ORF4, wherein the Ra12 nucleotide sequence is 5' to ORF4.

Upon perusal of SEQ ID NO: 1861 and 1862, it is noted that Example 10 reverses these sequences.

Thus, Wang et al. teaches nucleic acid encoding a fusion protein comprising Ra12 and a non-Mycobacterium tuberculosis polynucleotide, wherein the Ra12 polypeptide consists of SEQ ID NO:18 or SEQ ID NO:17 (note that here SEQ ID NO:18 comprises the full-length SEQ ID NO:17).

Watson et al. teach cDNA encoding mammaglobin as SEQ ID NO:1 (see Figure 2). Mammaglobin is a mammary-specific breast cancer protein antigen useful for immunotherapy-based method of treating breast cancer by inducing humoral and cell-mediated immune response against breast tumors.

It would have been obvious to a person having ordinary skill in the art to substitute the cDNA encoding L801P ORF4 or ORF 5 with the cDNA encoding mammaglobin antigen because Wang et al. teach that Ra12 enhances the expression and/or immunogenicity of heterologous polynucleotide/polypeptide sequences and Watson et al. teach that mammaglobin is a mammary-specific breast cancer protein antigen useful for immunotherapy-based method of treating breast cancer by inducing humoral and cell-mediated immune response against breast tumors (applied to the instant claims 1 and 6). The expression of a Ra12:mammoglobin fusion protein is predictable because Wang et al. provides two examples of Ra12 fusion protein expression.

Claim Rejections - Provisional Rejection, Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b). Effective 1 January 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 11 and 14-15 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-4 and 7 of copending Application No. 09780669. This is a provisional double patenting rejection because the conflicting claims have not in fact been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application

since the referenced copending application and the instant application are claiming common subject matter, as follows:

Claim 1 of Application 09780669 discloses an isolated polynucleotide of SEQ ID NO: 822 which is a fusion construct: Ra12-P510S-C (see [0601]) wherein P510S-C is a mammalian polynucleotide, i.e., non-*Mycobacterium tuberculosis* molecule (see [0935] and [0044]) and wherein the Ra12 sequence (nucleotides: 22-405) of SEQ ID NO:822 encodes the polypeptide identical to SEQ ID NO: 18 of the current invention and the Ra12 sequence is located 5' to the P510S-C sequence; and claims 2 and 7 of 09780669 set forth that P510S-C amino acid sequence of SEQ ID NO:826 (see [0605] and the patent claim 2) is a component of a fusion protein (see the patent claims 2 and 7). Thus, the 09780669 disclosure is an obvious variation of claims 1-2 and 11 of the current application.

Claims 3 and 4 of 09780699 set forth an expression vector comprising the above-mentioned polynucleotide operably linked to an expression control sequence (i.e., transcriptional regulatory element, see [0709]) and a host cell into which the expression vector is transferred. Claims 3 and 4 of 09706999 and the instant claims 14 and 15 thus disclose the common subject matter.

It is therefore concluded that the claims of the present application are not patentably distinct from the claims of Application No. 09780669.

Applicants' response to the rejections under 35 USC 102(e) and 35 USC 103(a))

The response filed 16 August 2004 argues that the primary reference, i.e., US Patent 6509448 is not qualified as a prior art to support the rejection under 35 USC 102(e) and 103(a)

because the most immediate priority document to 6509448, Application No. 09/702705 (now US Pat No. 6504010), does not sufficiently reveal disclosure as to SEQ ID NOs:1861-1864; and thus, 6509448 is entitled to only its actual filing date as its effective filing date (see pages 6-8).

The applicants' argument has been considered but it is found to be unpersuasive because the priority document, Application 09/702705 (i.e., the patent 6504010) does set forth nucleotide sequences and amino acid sequences of Ra12 referring as to US patent application 60/158585 (see column 51, the 3rd paragraph, of 6504010) form which the (provisional) application the current application claims a benefit. Thus, the skilled artisan will be directed by the description set forth in column 51 of 6504010, and entirely find SEQ ID NO:1862 which are the nucleotide sequences encoding SEQ ID NO: 1864 which are an amino acid sequences of Ra12 of 6509448 (i.e., Wang et al. patent) according to 60/158585. Thus, the disclosure of 6509448 is qualified as the prior art mentioned above.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on

the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Samuel Wei Liu, Ph.D.

October 5, 2004

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER